GUIDANCE DOCUMENT FOR PREPARING AN APPLICATION FOR THE CLINICAL SCIENCE RESEARCH & DEVELOPMENT SERVICE (CSR&D) COOPERATIVE STUDIES PROGRAM (CSP) COORDINATING CENTERS (CSPCC)
Described in Information Letter xx-2006-xxx

CONTENTS

Page

I. INSTRUCTIONS FOR INTENT TO SUBMIT NOTIFICATION

An e-mail attachment from the local VA Medical Center Research Office (ACOS for Research or Administrative Officer) with the Subject line "CSPCC Intent to Submit Notification" should be sent to CSP@va.gov with the following information:

(a) Proposed CSPCC Director Name, Degree, and VA appointment (in eighths)
(b) Proposed time commitment (CSPCC Director)
(c) VA Medical Center
(d) Title of proposal
(e) Keywords (up to six covering major topics areas and/or any special methodology)
(f) List of key personnel: Include names and area of expertise for at least 4 clinical trials, methodological/statistical and/or administrative experts at the center (for definition of key personnel, see II.3).
(g) Qualities that make the CSPCC personnel and activities a unique VA entity able to contribute to the CSP clinical trials infrastructure: (limit ½ page, single spaced)
(h) Summary of experiences in multi-site clinical trials and/or qualifications: (limit one page, single-spaced)

Due Date: The notification of intent to submit must be received by March 17, 2006.

A confirmation e-mail acknowledging receipt of intent to submit information will be sent to the local research office. This confirmation must be included as the last page of the full proposal when submitted.

Intent to submit notification from anyone other than the local VA Medical Center Director or facility research office personnel (e.g. the CSPCC Director, etc.) will not be accepted or acknowledged.

This information will be reviewed for responsiveness to the scope of the solicitation, for eligibility, and to plan for expertise needed in the review process.

II. CSP COORDINATING CENTER DESCRIPTION

1. VA Multi-site Clinical Trial Focus. Each Cooperative Studies Program Coordinating Center (CSPCC) will have a primary focus of conducting multi-site clinical trials within the VA Cooperative Studies Program. These studies are to provide definitive evidence for clinical practice that advances the health and healthcare of our veterans and the nation. CSPCCs must be able to conduct CSP research, operate in accordance to program policies, and provide leadership to the entire VA clinical research program. Furthermore, CSPCCs must be able to maintain their primary identity within the VA and specifically within the organizational structure of the Clinical Science Research & Development (CSRD) Service.

2. Director. The CSPCC Director is responsible for the coordination of all CSPCC activities and management of assigned studies. The Director must be a key member of the VA Medical Center research/clinical community and have a record of significant contributions to the VA research program in general. The CSPCC Director must have, at a minimum: a 5/8ths VA appointment; experience in managing clinical trials; and, knowledge about all aspects of conducting a multi-site clinical trial. A CSPCC Director should have particular expertise in trial design/methodology. A CSPCC Director is expected to play key national and local leadership roles in developing and implementing CSP initiatives, policies, and scholarship. Therefore, CSPCC Directors should have an established record of scientific, methodological/biostatistical, and/or clinical contributions and achievements that have advanced the clinical research arena. CSPCC Directors should also have a strong ability to lead and manage large-scale collaborative activities.

CSPCC Directors must be approved by the Director, CSRD. Given the organizational structure of the CSP, CSPCC Directors report directly to and receive ratings and performance evaluations from the Director, CSRD. CSPCC Directors who are clinicians (MDs) must be allowed to have the Director, CSRD concur with performance/evaluation ratings related to CSPCC activities and/or provide input into the local ratings by the clinical supervisor.

3. Coordinating Center Core Leadership.

a. There must be at least **four VA clinical trials experts** forming the core leadership for a CSPCC (CSPCC Core Leaders) who each have a minimum of a 5/8ths VA appointment. CSPCC leadership must also have a successful record of clinical research funding. These individuals can be one or more of the following:

(1) Biostatistician/epidemiologist – an expert with knowledge of advanced scientific principles in clinical trial design and statistical analyses. While doctoral level training is expected, individuals with masters level

training but significant experience in clinical trials may qualify; this expert must also have experience in providing leadership on clinical trials and be able to provide executive level direction/decision-making for multi-site trials.

(2) Clinical investigator/trialist – a clinician with clinical research experience who has a thorough understanding of key clinical trial methodological principles. This expert may have specific training in clinical research methodology and/or biostatistics, but it is not required; this individual must have had a history of obtaining clinical research funding and also be able to provide executive level direction/decision-making in conducting clinical multi-site trials.

(3) Senior administrator/manager – an expert with knowledge and experience in managing clinical trial operations, fiscal/accounting principles for multi-site clinical trials, and center management of personnel and/or activities; this individual should also have a thorough understanding of VA policies related to funding mechanisms, contracting, human resources, and/or other VA administrative activities.

4. Center Attributes. Proposed CSPCCs should have a thorough understanding and commitment to the VA research mission to enhance the health and care of our nation's veterans. Additionally, proposed CSPCCs must have an established history of designing, conducting and managing multi-site clinical trials. In particular, there should be a biostatistical/methodological core that is capable of rigorously designing and analyzing CSP studies and an administrative core that is able to handle study budgeting/accounting, human resources, and compliance for CSPCC and study activities. The biostatistical/methodological core should be comprised of individuals who will contribute to CSP methodological initiatives and ensure scientific excellence in all CSP activities. The administrative core must have expertise in budgeting and accounting for multi-site clinical trials and familiarity with relevant VA policies on personnel, meeting coordination, travel, and compliance. CSPCC personnel should also be able to manage all aspects of clinical trials including, but not limited to, project management, programming, form design, data collection/verification, quality assurance, document/record management and study reporting.

Proposed CSPCCs should have an overall environment that promotes study/research integrity, ownership, collaboration, and commitment to the veteran population. CSPCCs should have a system or plan for training/mentoring internally (i.e., within the center) and externally (i.e., local VA community, university affiliate, VHA). All CSPCC attributes should not only serve as key strengths of the center, but also for the entire CSP.

5. Management Attributes. While the CSPCC Director is primarily responsible for all center activities, multiple management activities occur at the center. Such activities are related to, but not limited to, CSPCC staff and workload, study activities, interactions with study chairs and principal proponents, and direct accountability to VA Central Office. Additionally, CSPCCs are responsible for ensuring that studies are conducted in a timely and efficient manner. Therefore, each CSPCC must have plans in place for systematically meeting CSP performance measures for study enrollment, adequately reaching important milestones and budgets, and reporting such progress. CSPCCs should have processes where excellence and accountability among all individuals (i.e., personnel, field investigators) involved in center activities are actively promoted.

Successful management also requires that proposed CSPCCs be able to maintain and leverage state-of-the art technology and technical expertise to enable the long-term viability of the center and the CSP. CSPCCs must also be able to establish meaningful collaborations with other CSP Centers so that resources are efficiently managed within the program.

Overall, proposed CSPCCs should have metrics for determining how they are achieving overall center and program goals.

6. Core Facilities. VA Medical Centers and VISNs must demonstrate a significant commitment to support CSPCC activities. This commitment must include the provision of physical space at the VA Medical Center that is sufficient for housing all activities, equipment, and products required in the conduct of multi-site clinical trials. Space for core facilities are to be supported without CSP funding. The goal of CSPCC-supported Core Facilities is to enhance collaborative interactions between investigators, staff, and other key individuals. Clinical cores may be established for study monitoring, data management and analysis, policy analysis, or other related activities to be used by multiple clinical studies. Laboratory core(s) used by multiple investigators for tissue banking, genetics, or molecular virology, etc., may be proposed.

Note: Proposed inclusion of these core facilities or any other specific aspect of a proposal does not mean that CSP will commit to funding them, even if the proposal is accepted.

7. Institutional Environment. In addition to VISN and VAMC-level facility support, the application should indicate other areas of support to be provided. Examples include, but are not limited to, salary support for CSPCC personnel, promotion of center activities/accomplishments, and/or growth opportunities provided. For proposed CSPCCs with a clinician director (MD), the local VAMC must be willing to allow the Director, CSRD to concur with performance evaluations on CSPCC responsibilities and/or provide direct input into these evaluations. Given the potential for industry collaboration on CSP studies, a strong relationship with the local VA non-profit corporation must be evident.

In accordance with the CSRD Service's emphasis on scholarship and leadership in clinical research, an environment that promotes a strong association with one or more academic affiliates is a critical element for a CSPCC. Evidence of these associations may include formal partnerships with the affiliate, faculty appointments for key CSPCC personnel, training opportunities, and/or the ability for accomplished non-VA personnel at the university to contribute to CSPCC scholarship/activities.

8. Center Initiatives / Innovations. The CSP has a distinguished history that is comprised of several examples of innovative approaches to clinical research. Some of these innovations include developing rigorous clinical trial methodologies, business practices in accounting and/or study management, human subjects protection, scientific/clinical advances, and technological advances. Proposed CSPCCs are expected to continue this innovative spirit by developing initiatives that are intended to move the VA clinical research program forward. While an individual CSPCC can take the lead in any given initiative, they should consider how such initiatives would be strategic in the context of any synergy provided by other centers, the CSP, and/or the entire VHA system. Partnerships with other clinical research groups that uniquely leverage the ability to advance veteran health care may also constitute important initiatives. While on-going efforts can be included in such innovations, applicants are expected to highlight new innovations that may lead to best practices in and/or scientific contributions to clinical research and the VHA healthcare mission. All innovations must also demonstrate CSPCC understanding of relevant VA policies and/or operating parameters.

9. Funding. CSPCCs do not apply for a specific budget level or amount of funding. The CSP utilizes a budgeting model where funding support is heavily provided on a per study basis. While core personnel may be supported, applicants must be able to demonstrate an ability to develop clinical trials and/or observational study protocols that would successfully merit funding by an independent scientific review board.

10. Restrictions. Since CSPCCs are part of the overall CSP infrastructure for conducting multi-site clinical trials, applicants must be able to demonstrate their ability to maintain a primary identity with the CSP. While non-VA sponsored activities are permitted at CSPCCs, all key center personnel must have a primary affiliation with the VA. Furthermore, CSPCCs must be able to conduct all center activities in accordance with VA/CSP policies and standards.

11. Evaluation. CSPCC proposals will be evaluated on the basis of the following major components:

a. Compliance with eligibility criteria;

b. Strength of the ability and approach of the proposed CSPCC in relation to meeting veterans' healthcare needs through multi-site clinical trials and related clinical research activities;

c. Scientific/managerial qualifications of the Director and CSPCC core leadership;

d. Attributes and qualifications for conducting multi-site clinical trials; these items include the proposed CSPCC's ability to operate within the context of VA/CSP policies, procedures, and standards;

e. Managerial processes for CSPCC activities, personnel, and other assets;

f. Commitment to the CSPCC by the VA Medical Center, VISN, and affiliated institution(s);

g. Core facilities that enable the full scope of multi-site clinical trial design, management, and analytical activities to be conducted;

h. Ability to foster strong collaborative ties with and/or be successful in collaborative interactions with other CSP Centers and clinical research groups;

i. Ability to provide leadership for the VA clinical research program;

j. Plans for developing innovative approaches to the conduct of clinical research, particularly within the context of the CSP.

12. <u>Annual Performance Review</u>. Each CSPCC is required to submit to VA Central Office an annual research performance report. Performance measures include:

a. Importance of major research findings from the CSPCC;

b. Productivity as indicated by the number of publications and new funding awards directly attributable to CSPCC core activities;

c. Study management including meeting projected milestones, patient accrual, and/or fiscal accountability. For research activities involving one or more non-VA collaborators, study management includes an ability to manage outside funding;

d. CSPCC accountability to Central Office and adherence to CSP policies;

e. Scientific and/or methodological contributions to the clinical research field;

f. Evidence of local, national, and international recognition of the CSPCC and/or its members; and

g. Contributions of the CSPCC to the overall CSP mission and initiatives.

***NOTE**: Unsatisfactory performance will result in probationary status or termination of funding.*

III. CALENDAR FOR CSPCC REVIEW AND FUNDING

Notification of Intent to Submit Deadline E-Mail to: CSP@va.gov	March 17, 2006
Full Application Deadline Send to: VA Office of Research & Development Cooperative Studies Program (125) **Attn: CSPCC Applications** 810 Vermont Avenue, NW Washington, DC 20420 Phone: (202) 254-0183	May 31, 2006
Scientific Review	Summer 2006
Funding Start Date	October 1, 2006

IV. INSTRUCTIONS FOR PREPARATION OF CSPCC APPLICATIONS

1. Submit the original application plus twelve copies of the application, duplicated on 8.5 x 11 inch white paper. Except for the original, which needs to be duplicated face only, all forms and narrative material need to be duplicated back-to-back. Use a blank sheet of paper as a continuation sheet for the forms where necessary. CSRD, Department of Veterans Affairs (VA) Central Office uses the original as the master file copy. Type material single-spaced, leaving a 1 inch margin at each edge of each sheet. Do not use small fonts, submit applications prepared from a dot matrix printer, or use photo reduction. Type the name of the center location in the lower right portion of each numbered page.

2. The application needs to be complete and comprehensive as submitted. Applications are considered incomplete and will be returned if they are illegible, fail to follow instructions, or if the material presented is insufficient to permit an adequate review. CSPCC applications must conform to a standardized format as outlined so that each application contains all of the pertinent information. This requirement is critical to a comparative review of the applications. Limit the narrative to twenty-five pages (see Roman numerals I-VII). Do not submit copies of funded or pending research applications of investigators. Each CSPCC Core Leader may submit up to two reprints representing their most important work. Submit six collated sets of these reprints.

3. The first pages of the application should be Department of Veterans Affairs (VA) Form 10-1313-1, Merit Review Application, and VA Form 10-1313-2, Summary Description of Program, followed by a Table of Contents with page numbers. Instructions for preparation of the 10-1313 forms may be obtained from Appendix A of the draft VHA Handbook for BLR&D/CSR&D Merit Review at the following website: http://www.research.va.gov/resources/policies/docs/1202_Merit_Review_Handbook_JIT.doc Use the following designated roman numerals and headings:

I. Background of the CSPCC

II. Research Focus

III. Personnel

IV. Center Attributes & Facilities

V. Resources

VI. Institutional Environment

VII. New Initiatives

VIII. Letters of Endorsement and Support

IX. Budget. VA Forms 10-1313-3, Current Funds and First Year Request for Program, and VA Form 10-1313-4, Estimated Expenses of Program

X. Appendices. Under Appendices, list the following:

A. VA Form 10-1313-5/6, Combined Investigator's Biographic Sketch and Bibliography, limit two pages for each investigator.

B. VA Form 10-1313-8, Summary Statement, Abstract and Budget Summary, for each VA and Non-VA funded proposal for each CSPCC Core Leader.

C. Other relevant information.

4. Based on the headings listed above, the main narrative on the proposed CSPCC should be provided according to the following. The CSPCC proposal should address all sections indicated below and specifically include elements given in the CSP Coordinating Center Description section. Only items I-VII are counted toward the 25-page limit for the proposal.

I. Background on the Center. Address the history and background of the proposed CSPCC and its interaction with your VA Medical Center and affiliated university(ies) in the area of clinical research and multi-site clinical trials.

II. Research Focus. Describe the research focus and goals of the CSPCC. Accomplishments in the multi-site clinical trials arena, collaborations, studies/projects, awards, and other major contributions to clinical research should be included in this narrative. Any description of a research portfolio should provide details of the level of complexity (e.g., federal/industry collaborations) and diversity of studies (e.g., small/large projects, observational studies, randomized single- or multi-site controlled trials). On-going and/or future directions for how the research activities at the CSPCC would contribute to the CSP mission to advance veteran health and healthcare should also be highlighted.

III. Personnel. List the name, academic title, VA title, and VA employment status (in VA paid 8ths) for key CSPCC personnel. Each individual should have a brief narrative of his/her qualifications in the context of multi-site clinical trials. These descriptions can include, but are not limited to, funded research and other relevant experience to the primary duties of the proposed CSPCC. Participation on VA/NIH committees, national honors and awards and other prominent clinical research positions may be included. Other technical and support staff that would be involved in CSPCC activities can be briefly described.

IV. Center & Management Attributes. Describe the ability of the proposed CSPCC for carrying out CSP activities. This description should specifically include biostatistical and administrative capabilities. Management attributes and other practices essential to the operation of a CSPCC should also be detailed. Particular emphasis should be placed on center and management attributes described in Paragraphs 4 & 5 under CSP Coordinating Center Description.

V. Resources. Physical facilities for where the CSPCC is to be housed should be described and how they are conducive to fulfilling CSP responsibilities. Describe the research facilities available, both within the VA Medical Center and through affiliated institutions. Distinguish between those resources that are currently in place, and those resources that must be added to fulfill the CSPCC mission. If support for a core facility is requested, explain how a specialized core laboratory strengthens the activities of the CSPCC.

If a Clinical or Epidemiological Core Facility is requested, briefly describe ongoing studies by investigators or proposed clinical and/or epidemiological studies at the Center that would benefit from the proposed core(s), including description of the patient population, number of subjects, duration of study, and number of samples if relevant. In Appendix C, include the abstracts and more comprehensive description of the studies.

VI. Institutional Environment. Describe the local VA and the academic environment at the proposed CSPCC. This description should not only include level/amount of leadership support, but explain any relationships and plans involving the proposed CSPCC and the VA leadership and university affiliate(s). Details for how such relationships will be beneficial to the CSP mission should be provided.

VII. New Initiatives. CSPCC awards are intended to provide an added dimension to the CSP's ability to meet its mission and to create a synergistic relationship among all entities within the program. An explanation of how this expectation will be met is critical to the establishment of the CSPCC. Describe any innovations and initiatives that would contribute to the CSPCC's ability to meet center goals and the CSP's ability to continue its leadership in clinical research. Any special advantages the CSPCC provides to building the program should be highlighted.

VIII. Letters of Endorsement and Support. Include letters of endorsement from the Medical Center Director and Veterans Integrated Services Network (VISN) Director. Include a letter of endorsement from the Research and Development Committee. Letters of support from the affiliated institution and relevant department chairperson(s) are optional, but helpful. Letters of support from other collaborators (e.g., investigators, institutes, agencies) may also be included if desired.

IX. Budget. Use VA Form 10-1313-3, R&D Program – Current Funds & First Year Request, and VA Form 10-1313-4, R&D Program Estimated Expenses, to summarize and justify the requested budget. Request only resources and facilities directly identified with the Center. Allowable categories are as follows:

a. Initial costs for technical personnel essential to maintain core or shared facilities. NOTE: Costs for staff supported by individual research awards are not allowed.

b. Specialized Shared Core Equipment. If a major equipment item or specialized facility is requested, justify thoroughly and include documentation of in-kind partnering and/or direct contributions by the VA Medical Center, affiliated institution, or other sources.

c. Supplies and operating costs for core laboratories.

d. Center infrastructure support, such as maintenance contracts on core equipment.

e. Other miscellaneous expenses.

Note: A successful CSPCC proposal does not guarantee that all funding requests in the application will be made nor is there a CSP commitment to core laboratories/equipment. Rather, CSPCC selections will enable a process where negotiations with VA Central Office can occur for center budgets.

X. Appendices

Appendix A. Include VA Forms 10-1313-5/6, Combined Biographical Form, for each CSPCC Core Leader, followed by the same form for other participating investigators. Limit the bibliography to two pages per investigator.

Appendix B. Include VA Form 10-1313-8, Investigator's Total VA & Non-VA Research Support, for each scientific CSPCC Core Leader (Director, biostatisicians/methodologists, clinical investigators/trialists). Include VA Form 10-1313A, Merit Review Board Summary Statement, or other funding agency front sheet, abstract and budget summary for each Federal and non-Federal funded proposal for each scientific CSPCC Core Leader.

Appendix C. Include other relevant information.

5. **Due Date.** The application is due in VA Central Office by May 31, 2006.

6. **Application Submission.** The application should to be sent through the VA Medical Center Research and Development Office, the Research and

Development Committee, the Medical Center Director and other appropriate channels for transmittal to VHA Central Office.

a. Submit to VHA Central Office:

(1) The original application,

(2) Twelve copies of the application (without Social Security Numbers), and

(3) Six collated sets of reprints (2 reprints per investigator).

b. Applications should be sent by UPS or couriers (e.g. Fed Ex) to:

VA Office of Research & Development
Cooperative Studies Program (125)
Attn: CSPCC Applications
810 Vermont Avenue, NW
Washington, DC 20420
Phone: (202) 254-0183

V. CHECKLIST FOR CSPCC APPLICATIONS

_____1. Front sheet Department of Veterans Affairs (VA) Form 10-1313-1, Merit Review Application, signed by the Associate Chief of Staff Research and proposed CSPCC Director (PI).

_____2. Abstract of the application, i.e., VA Form 10-1313-2, Summary Description of Program.

_____3. Table of Contents with page numbers.

_____4. List of abbreviations.

_____5. Narrative. A maximum 25 pages containing items I-VII.

_____6. Letters of Endorsement from the Medical Center Director and Veterans Integrated Service Network (VISN) Director.

_____7. Letter of Endorsement from the Research and Development (R&D) Committee.

_____8. Other letters of support.

_____9. First year budget for the program; use VA Form 10-1313-3, Current Funds and First Year Request for Program.

_____10. Budget summary and justification; use VA Form 10-1313-4, Estimated Expenses of Program.

_____11. Documentation of support from VA Medical Center, VISN and/or affiliated institution for shared equipment or core facilities.

_____12. VA Form 10-1313-5/6, Investigator's Biographic Sketch and Bibliography for each CSPCC Core Leader. NOTE: Limit the bibliography to two pages per investigator.

_____13. VA Form 10-1313-8, Summary statement, abstract and budget for each federal and non-federal funded proposal for each scientific CSPCC Core Leader. Identify the investigator on each abstract.

_____14. Confirmation of receipt of email notification of intent to submit

_____15. Twelve copies of the application (with social security numbers redacted).

_____16. Six collated sets of reprints (two reprints).

_____17. Appendices